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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/988,150 | 11/19/2001 | Dario Cremaschi | 216261US0CONT | 8275 |

22850 7590 03/09/2005

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| EXAMINER | |
|---|---|
| NICKOL, GARY B | |
| ART UNIT | PAPER NUMBER |
| 1642 | |

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/988,150 | CREMASCHI ET AL. | |
| | Examiner | Art Unit | |
| | Gary B. Nickol Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *11-13,15-22 and 24-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *22 and 24-28* is/are allowed.

6)☒ Claim(s) *11-13 and 15-19* is/are rejected.

7)☒ Claim(s) *20 and 21* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Cremaschi et al

Date of priority: 04-14-1997

Claims 11-13, 15-22, 24-28 are pending.

## DETAILED ACTION

Upon review and reconsideration, the finality of the previous office action mailed 04-09-2004 is withdrawn.

**New Rejections/Objections:**

### *Claim Objections*

Claims 12 and 21 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claims 12 (and 21) recite the method of Claim 11 (or Claim 20), wherein said protein is selected from the group consisting of "polypeptides". The specification does not appear to differentiate between a "protein" and "polypeptides". Thus, claim 12 does not further limit the subject matter of claim 11. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-13, and 15-19 are rejected under 35 USC 103(a) as being unpatentable over Smith *et al.* (WO94/28879, IDS) in view of U.S. Patent No. 5,879,712 (Bomberger *et al.*, June 1995) and Almeida *et al.* ("Nasal Delivery of Vaccines", Jnl. of Drug Targeting, 1996, Vol. 3, pages 455-467, *copy enclosed with previous actions*)

The claims are broadly drawn to a method for intranasally administering a composition comprising a microparticle having a protein and an antibody adsorbed thereon, wherein said administering comprises contacting a microparticle having a protein and an antibody thereon with the nasal mucosa of a patient in need thereof, wherein said antibody is an immunoglobulin specific for the protein (Claim 11), wherein said protein is selected from the group consisting of BSA, insulin, enkephalin, hormones, growth factors, cytokines, coagulation factors,

polypeptides, and antimicrobial agents (Claim 12); wherein said antibody is an immunoglobulin selected from the group consisting of IgM, IgA, and IgG (Claim 13); wherein said microparticle is biodegradable (Claim 15); wherein said microparticle comprises polystyrene (Claim 16); wherein the ratio of protein to antibody is 1 to 15, 000 moles of protein per mole of antibody (Claims 17), 1 to 5000 moles of protein per mole of antibody (Claim 18), or 1 to 100 moles of protein per mole of antibody (Claim 19).

1. Smith teaches a method for administering a composition comprising a microparticle having a protein and an antibody adsorbed thereon, wherein said administering comprises contacting a microparticle having a protein and an antibody thereon for oral administration (see abstract); wherein said protein is selected from the group consisting of BSA, insulin, enkephalin, hormones, growth factors, cytokines, coagulation factors, polypeptides, and antimicrobial agents (see page 6); wherein said antibody is an immunoglobulin selected from the group consisting of IgM, IgA, and IgG (see page 3); wherein said immunoglobulin is specific for the protein (see page 4) wherein said microparticle is biodegradable (see page 7); wherein said microparticle comprises polystyrene (see page 8); wherein the ratio of protein to antibody is 1 to 15, 000, 1 to 5000, or 1 to 100 moles of protein per mole of antibody (see page 19).

2. Smith *et al.* do not teach *intranasal* administration of the microparticle.

3. Bomberger *et al.* (US Patent No. 5,879,712) teach the intranasal administration of microparticles loaded with biologically active drugs, including proteins such as ICAM-1 (abstract, column 1, lines 20+, column 4, lines 45+)

4. Almeida *et al* teach that microparticles can act as carriers for antigens delivered by the nasal route (page 462, 2nd column, page 463, 1st column). Almeida *et al.* further teach that "intranasal immunization appears the *superior* route to achieve a comprehensive immune response" wherein the advantages of nasal delivered medicines (compared to other mucosal surfaces) include the valuable mucosal surface of approximately 150 $cm^2$, the accessibility and easy administration that increases patient compliance, and a highly vascularized and venous flow that escapes the portal system, thus preventing first-pass metabolism in the liver (page 457, 1st column).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include nasal administration of the composition taught by Smith *et al.* because nasal administration of microparticles containing peptides and proteins was well established in the art as taught by Bomberger *et al.* (US Patent No. 5,879,712) and Almeida *et al.* Further, one would have been motivated to do so because Almeida *et al.* teach that nasal delivered vaccines are advantageous compared to other mucosal surfaces because of the valuable surface area of the nasal mucosa, the easier accessibility and administration that increases patient compliance, and a highly vascularized and venous flow that bypasses the portal system, thus preventing first-pass metabolism in the liver (page 457, 1st column). Thus, given the state of the

art, success, and advantages of intranasal administration of microparticles, it would have been obvious to include nasal delivery of the claimed compound, and one of ordinary skill in the art would have a reasonable expectation of success in administering the claimed compound via the nasal passageway.

Claims 22, and 24-28 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GARY NICKOL
PRIMARY EXAMINER
3/7/05

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